CLAIMS

What is claimed is:

1. A method of identifying a cyclic peptide capable of altering a phenotype of a cell, comprising the step of:

administering to the cell a cyclic peptide comprising a chaperone binding region of known sequence and a target binding region of wholly or partially unknown sequence; and

assessing whether a phenotype of the cell has been altered.

2. The method of Claim 1 in which the cyclic peptide is composed wholly of gene-encoded amino acids.

3. The method of Claim 1 in which the chaperone binding region binds an immunophilin.

4. The method of Claim 3 in which the immunophilin is cyclophilin or an FK-binding protein.

5. The method of Claim 4 in which the cyclophilin is selected from the group consisting of cypA, cypB, cyC and cycD.

6. The method of Claim 4 in which the FK-binding protein is selected from the group consisting of FKBP12, FKBP13, FKBP25 and FKBP59.

7. The method of Claim 3 in which the immunophilin is endogenous to the cell.

8. The method of Claim 3 in which the immunophilin is exogenous to the cell.

9. The method of Claim 1 in which the chaperone binding region has an amino acid sequence selected from the group consisting of Ala-Gly-Pro-Ile and Leu-Pro.

10. The method of Claim 1 further including the step of determining the sequence of the target binding region of the cyclic peptide.

11. The method of Claim 1 in which the target binding region of the cyclic peptide is composed of from 4 to 10 amino acid residues.

12. The method of Claim 1 in which the chaperone binding region and the target binding region of the cyclic peptide are contiguous.

13. The method of Claim 1 in which the chaperone binding region and the target binding region of the cyclic peptide are spaced apart from one another via linkers, which may be the same or different.

14. A method of identifying a cyclic peptide capable of altering a phenotype of a cell, comprising the steps of:

administering to a plurality of cells a plurality of cyclic peptides, each of which comprises a chaperone binding region and a target biding region;

identifying those cells exhibiting an altered phenotype (positive cells); and

determining the sequence of at least the target binding region of the cyclic peptides of positive cells.

15. The method of Claim 14 in which the chaperone binding region of each cyclic peptide of the plurality is the same.

16. The method of Claim 14 in which each the target binding region of each cyclic peptide of the plurality includes a unique random sequence ranging from 4 to 10 amino acids in length.

17. The method of Claim 14 in which the chaperone binding region binds an immunophilin.

18. The method of Claim 17 in which the immunophilin is endogenous to the cells.

19. The method of Claim 17 in which the immunophilin is exogenous to the cells.

20. The method of Claim 17 in which the immunophilin is a cyclophilin.

21. The method of Claim 17 in which the immunophilin is an FK binding protein.

22. A method of isolating a target capable of altering a phenotype of a cell, comprising the steps of:

administering to a cell expressing a chaperone a cyclic peptide comprising a region capable of binding the chaperone and a target binding region of wholly or partially unknown sequence;

if the cell exhibits an altered phenotype, contacting a lysate of the cell with an affinity reagent capable of specifically binding a the chaperone; and

dissociating and isolating any target bound to the chaperone.

23. The method of Claim 22 in which the chaperone is an immunophilin.

24. The method of Claim 23 in which the affinity reagent comprises an anti-immunophilin antibody.

25. The method of Claim 22 in which the affinity reagent is immobilized on a solid support.

26. The method of Claim 22 which further includes the step of determining the identity of the isolated target.

27. A method of identifying a target capable of altering a phenotype of a cell, comprising the steps of:

administering to each of a plurality of cells a cyclic peptide comprising a chaperone binding region and a unique target binding region;

isolating a cell exhibiting an altered phenotype;

contacted said isolated cell with an affinity reagent that specifically binds the chaperone;

isolating there from any bound target; and

determining the identity of the isolated target.

28. A cyclic peptide composed of from 4 to 30 amino acids, comprising:

a chaperone binding region; and

a target binding region of wholly or partially unknown sequence.

29. The cyclic peptide of Claim 28 which is composed wholly of gene-encoded amino acids.

30. The cyclic peptide of Claim 28 in which the target binding region is a random sequence.

31. The cyclic peptide of Claim 28 which has the formula:

cyclo(Ser-X^2-X^3-X^4-X^5-X^6-X^7-X^8-X^9-L^1-Y^1-Y^2-Y^3-Y^4-L^2)

wherein:

X^2-X^9 are each, independently of one another, a gene-encoded amino acid, with the proviso that from 1 to 5 of X^2-X^9 may be absent;

L^1 is an optional linker composed of gene-encoded amino acids;

Y^1-Y^4 taken together comprise the chaperone binding region; and

L^2 is an optional linker composed of gene-encoded amino acids.

32. The cyclic peptide of Claim 31 in which Y^1-Y^4 is selected from the group consisting of AGPI and LP.

33. A library of cyclic peptides, each of which comprises a chaperone binding region and a target binding region, wherein the target binding region of each cyclic peptide is unique.

34. The library of Claim 33 in which the chaperone binding region of each cyclic peptide is the same.

35. The library of Claim 33 in which the target binding region is composed of from 4 to 10 amino acid residues.

36. The library of Claim 35 which comprises from 20^4 to 20^{10} members.

37. A polynucleotide capable of expressing a cyclic peptide comprising:

a first segment encoding a C-terminal intein domain;

a second segment encoding a linear version of cyclic peptide, said cyclic peptide comprising a chaperone binding region and a target binding region; and

a third segment encoding an N-terminal intein domain, wherein the first, second and third segments are arranged such that the polynucleotide expresses a cyclic peptide.

38. The polynucleotide of Claim 37 which is single stranded.

39. The polynucleotide of Claim 37 which further includes an inducible promoter operably linked to the first segment.

40. The polynucleotide of Claim 37 in which the cyclic peptide further includes linkers intervening the chaperone binding region and the target binding region.

41. A library of polynucleotides capable of expressing cyclic peptides, each polynucleotide of the library comprising:

a first segment encoding a C-terminal intein domain;

a second segment encoding a linear version of a cyclic peptide, said cyclic peptide comprising a chaperone binding region and a target binding region; and

a third segment encoding an N-terminal intein domain, wherein said first, second and third segments are arranged such that the polynucleotide is capable of expressing

the cyclic peptide and wherein the target binding region of each expressed cyclic peptide is unique.

42. A host cell comprising a polynucleotide according to Claim 41, or progeny thereof.

43. The host cell or progeny of Claim 42 in which the polynucleotide is integrated into the genome of the cell or progeny.

44. A library of cells in which each cell of the library comprises a polynucleotide capable of expressing a cyclic peptide comprising a chaperone binding region of known sequence and a target binding region of wholly or partially unknown sequence, wherein each cell comprises a unique polynucleotide.